M E M O R A N D U M

TO: JAMES T. NEWSOM (EXT. 3060)

FROM: SALLY MERRIAM (EXT. 2559)

DATE: AUGUST 29, 1989

RE: PASSIVE SMOKING AND PERIPHERAL VASCULAR DISEASE

CC: DONALD K. HOEL -- WITHOUT ATTACHMENT
ANTHONY J. ANDRADE -- WITH ATTACHMENT
WILLIAM W. DAVIS (EXT. 2622) -- WITHOUT ATTACHMENT

Many papers have attempted to link passive smoking (ETS) with some form of cardiovascular disease, including but not limited to ischemic heart disease (IHD), coronary vessel disease (CVD), and peripheral vascular disease (PVD). Most notable among these attempts are Hirayama's 1983 paper: "Lung Cancer in Japan. Effects of Nutrition and Passive Smoking," which reported a significant risk elevation for IHD in non-smoking women married to smokers. Neville Woolf's chapter entitled; "Cigarette Smoking and Atherosclerosis" in Roger Greenhalgh's 1982 book; Smoking and Arterial Disease, attempts to explain the mechanism by which active cigarette smoking causes adverse cardiovascular effects but does not prove a causative association. Chiyoji Ohkubo's 1982 paper: "Some Acute Cardiopulmonary Effects of Mainstream and Sidestream Cigarette Smoke in Man", found that sidestream smoke was more irritating than mainstream smoke. Furthermore, the paper found that because nicotine from sidestream smoke has a higher pH value than nicotine in mainstream smoke, it is more readily absorbed through the mucous membranes. It must be remembered that this paper considered acute effects only and not long-term effects or possible mechanisms of atherogenesis. Ohkubo stated that although the nicotine uptake by passive smokers was less than 1% of the amount taken in by smokers (estimated to be 14μg in smokers), constriction of peripheral blood vessels with a 1-2 second latency and which subsided within 2 minutes was observed. He conceded however, that the amount of nicotine was insufficient to cause changes in blood pressure or heart rate (page 183). [NOTE: Remember that increased systolic pressure is considered to be more important in atherogenesis than vessel constriction.]

The constituents of tobacco smoke most often implicated in causing adverse effects on the cardiovascular system are carbon monoxide (CO) and nicotine. Schievelbein's 1984 paper: "The In-

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fluence of Passive Smoking on the Cardiovascular System" (see attached), is probably the most succinct treatise on the subject, even though it discusses IHD and CVD with only minimal attention to PVD. CO as a mediator of intimal (artery lining) injury inducing increased endothelial permeability and resultant atherosclerosis has been studied by many workers. In 1970, Astrup and his colleagues reported increased cholesterol accumulation in the aortic wall of rabbits exposed to 200 ppm of CO for several weeks. Not only does this dose far exceed the estimated 5 ppm CO in indoor air originating from tobacco smoke, subsequent experiments by Armitage, et al. in 1976 and Astrup, et al. in 1978 failed to reproduce the results. Other animal studies on species such as monkeys, rabbits and pigeons have found no structural arterial lesions nor lipid depositions with exposure to experimental doses of CO. Thus, the theory that CO is an important factor in the pathogenesis of atherosclerosis has neither been proven nor disproven.

Similarly, animal studies on the chronic effects of nicotine have neither proven nor disproven an atherosclerotic sequelae. Nicotine has been implicated as a mediator in atherogenesis by mechanisms of its vasoconstrictive effect on peripheral blood vessels. Additionally, it has been theorized that nicotine-induced release of epinephrines produces an increase in the plasma concentration of free fatty acids. Catecholamine-mediated lipolysis has been implicated in the production of endothelial cell injury which would in turn increase endothelial permeability. Furthermore, nicotine-induced release of epinephrine has been suggested as a mediator in formation of microthrombi by its effect on platelet function and coagulation. The aforementioned roles of nicotine in atherogenesis has been studied and discussed only in regards to active smoking. Nicotine's acute effects from sidestream smoke is discussed in Ohkubo's paper as previously mentioned. This paper determined that nicotine in doses from sidestream smoke are not sufficient to induce the release of catecholamines such as epinephrine nor stimulate autonomic ganglia. Therefore, although nicotine can be implicated in the atherogenetic pathway in active smokers, its effect of peripheral vascular constriction is not sufficient to produce atherosclerosis in passive smokers because without the concomitant rise in blood pressure, endothelial injury, and increased platelet aggregation, the proposed pathogenic mechanisms for production of atherosclerosis are not complete.

Schievelbein's paper from which most of the information in this memorandum has been gleaned, discusses coronary heart disease specifically and may not be germane to the Fernandez case of PVD. Furthermore, most of the information discussed in Schievelbein's paper as well as other papers on passive smoking such as Hugod's 1981 paper entitled: "Passive Smoking", discuss the effects of carbon monoxide and nicotine in healthy passive

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smokers. Hugod's paper briefly discusses increased carbon monoxide concentration effects in individuals with pre-existing cardiovascular disease but the effects discussed involved only coronary heart disease and not PVD. Therefore, there are few, in any, studies known to date that discuss chronic passive smoking effects on peripheral vascular disease with pre-existing cardiovascular anomalies such as hypertension or other diseases such as diabetes. In conclusion of the literature reviewed to date, the effects of uptake of carbon monoxide and nicotine by passive smokers have no detectable physiological effect that can be determined to be inherent in atherogenesis.

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Appendix -- Some Facts and Figures:

1. Carbon monoxide (CO) concentration from tobacco smoke indoors equals approximately 5 to 40 ppm.

2. Carboxyhemoglobin (COHb) in smokers equals approximately a 3 to 10 percent increase over normal levels.

3. COHb concentration in non-smokers exposed to 20 to 30 ppm CO, increases from a normal of 0.7 to 0.9 percent to 1.6 to 2.6 percent COHb.

4. COHb concentration in non-smoking city dwellers is greater than 1.5%.

5. Nicotine levels in a room with smokers range from 5 to 50 $\mu g/m^3$.

6. Nicotine uptake by passive smokers is 1 to 2 percent of that by smokers.

SMH:crg

Attachments

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